Remarks

Reconsideration and withdrawal of the rejections of the claims, in view of the remarks presented herein, is respectfully requested. Claims 33-50, 53, and 54 are pending.

The Rejections under 35 U.S.C. § 103

The Examiner rejected claims 33-36, 39-50, 53 and 54 under 35 U.S.C. § 103(a) alleging that the claims are unpatentable over Hiraoka, Nature, 342: 293-296 (1989), in view of Abken, Cancer Journal, 8(3): 94-102 (1995). This rejection is respectfully traversed.

The Examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. In re Fine, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d (BNA) 1596, 1598 (Fed. Cir. 1988). If the Examiner does not establish a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness. To establish a *prima facie* case of obviousness, three criteria must be met. First, the prior art reference (or references) must teach or suggest all of the claim limitations. Second, there must be some suggestion or motivation, either in the cited reference (or references), or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Third, there must be a reasonable expectation of success. M.P.E.P. § 2142 (citing In re Vaeck, 947 F.2d 488, 20 U.S.P.Q.2d (BNA) 1438 (Fed. Cir. 1991)).

Claim 33

Claim 33 is the only independent claim as claim 50 has been amended to depend from claim 33. All other pending claims are dependent on claim 33.

Claim 33 relates to a method to identify an agent that increases or decreases the amount of double minute chromosomes or extrachromosomal DNA in a cell, comprising contacting the cell with the agent, wherein the cell expresses a labeled protein that associates with double minute chromosomes or extrachromosomal DNA to form a labeled complex; and comparing the amount of the labeled complex contained in the cell contacted with the agent with the amount of labeled complex contained in a cell that was not contacted with the agent.

Hiraoka et al., Nature, 342:293 (1989)

Hiraoka discloses that chromosomes in living *Drosophila* embryos were visualized by conjugating calf thymus histones H2A and H2B with rhodamine *in vitro* and then microinjecting the labeled histones into *Drosophila* embryos (page 293).

Abken, Cancer Journal, 8:94 (1995)

Abken discloses that recent experimental observations indicate that treatment of tumor cells with agents that accelerate the loss of extrachromosomally amplified genes in double minute chromosomes altered the growth phenotype and reduced the tumorigenicity of the cells (page 101). Abken also discloses that therapeutic agents that eliminate extrachromosomal double minute DNA may provide valuable tools for moderating the growth of a large number of human neoplasms (page 101).

Neither Hiraoka or Abken, alone or in combination, disclose or suggest (1) a method to identify an agent that increases or decreases the amount of double minute chromosomes or extrachromosomal DNA in a cell, (2) use of a cell that expresses a labeled protein that associates with double minute chromosomes or extrachromosomal DNA to form a labeled complex, or (3) comparing the amount of the labeled complex contained in a cell contacted with an agent with the amount of labeled complex contained in a cell that was not contacted with the agent.

The presently claimed method utilizes a cell that expresses a labeled protein that associates with double minute chromosomes or extrachromosomal DNA to form a complex. In contrast, the method disclosed by Hiraoka is for visualizing chromosomes by microinjecting labeled histones into embryos. Abken discloses detection of double minute chromosomes by cytogenetic methods. Thus, Applicants submit that there is no reasonable expectation of success that labeled histones would allow for detection of double minute chromosomes or extrachromosomal DNA. Furthermore, even if Hiraoka and Abken were combined, they would not disclose or suggest the claimed method of utilizing a cell that expresses a labeled protein, in distinction with microinjection of a labeled protein. Accordingly, the Examiner is respectfully requested to withdraw the rejections of the claims under 35 U.S.C. § 103.

The Examiner rejected claims 33-38, 42-50, 53 and 54 under 35 U.S.C. § 103(a) alleging that the claims are unpatentable over Robinett et al., Journal of Cell Biology, 135(6):1685-1700 (1996), in view of Abken, Cancer Journal, 8(3):94-102 (1995). This rejection is respectfully traversed.

Robinett et al., Journal of Cell Biology, 135:1685 (1996)

Robinett discloses a method that was used to visualize chromosomes in Chinese hamster ovary cells and in yeast (abstract). The method involved inserting 256 direct repeats of the lac operator into a chromosome, expressing a green fluorescent protein-lac repressor-nuclear localization signal fusion protein within the cell, and detecting the fusion protein bound to the lac operator inserted in the chromosome (Figure 1, page 1687).

Abken, Cancer Journal, 8(3):94-102 (1995) has been previously described.

Neither Robinett or Abken, alone or in combination, disclose or suggest (1) a method to identify an agent that increases or decreases the amount of double minute chromosomes or extrachromosomal DNA in a cell, (2) use of a cell that expresses a labeled protein that associates with double minute chromosomes or extrachromosomal DNA to form a labeled complex, or (3) comparing the amount of the labeled complex contained in a cell contacted with an agent with the amount of labeled complex contained in a cell that was not contacted with the agent.

Robinett discloses labeling chromosomes using chromosomally integrated lac operators and a tagged lac repressor. The tagged lac repressor does not associate with chromosomes, double minute chromosomes, or extrachromosomal DNA which do not include an integrated lac operator. It is only the presence of an integrated lac operator which allows the lac repressor to bind to, and label the chromosome. Robinett not only does not disclose the use of a labeled protein that associates with double minute chromosomes or extrachromosomal DNA, but teaches away from such a method by disclosing the need for the integration of a binding partner (lac operator) prior to use of the labeled protein (lac repressor). Abken discloses cytogenetic detection of double minute chromosomes and does not correct the deficiency of Robinett or

change its teaching. Thus, the combination of Robinett and Abken does not disclose or suggest the current invention. Accordingly, the Examiner is respectfully requested to withdraw the rejections of the claims under 35 U.S.C. § 103.

Conclusion

Applicants respectfully submit that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (612-371-2123) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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By their Representatives,

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Date June 5, 2003 By _____
Leif Stordal
Reg. No. 46,251

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, Washington, D.C. 20231, on this 5th day of March, 2003.

Name Dawn M. Poole Signature _____